



DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Food and Drug Administration
Los Angeles District
Pacific Region
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Irvine, CA 92612-2445

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WARNING LETTER

**CERTIFIED MAIL
RETURN RECEIPT REQUESTED**

February 15, 2005

W/L 11-05

Roger A. Roberts
Vice President and General Manager
Medsep Corporation, A Subsidiary of Pall Corporation
1630 West Industrial Park Street
Covina, CA 91722

Dear Mr. Roberts:

During an inspection of your medical device firm located in Covina, California, from August 2, 2004 to September 9, 2004, our investigators determined that Medsep Corporation (hereinafter "the firm" or "you") manufactures and distributes both devices and drugs.

The Bacterial Detection System (BDS) and the Enhanced Bacterial Detection System (eBDS) are intended for use with the Pall BDS Oxygen Analyzer in qualitative procedures for the recovery and detection of aerobic and facultative anaerobic microorganisms (bacteria) for quality control testing of leukocyte reduced apheresis or whole blood derived platelet units. These products are devices as defined by Section 201 (h) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. § 321(h)].

Our inspection disclosed that the devices are adulterated within the meaning of Section 501(h) of the Act, 21 U.S.C. § 351(h), in that the methods used in, or the facilities or controls used for manufacturing, packing, and storage are not in conformance with the **Good Manufacturing Practice (GMP) requirements for the Quality System Regulation**, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1. Failure to establish corrective and preventive actions (CAPA) procedures for investigating the cause of nonconformities relating to product, processes and the quality system [21 CFR 820.100(a)(2)]. Specifically, the firm received numerous customer complaints related to BDS performance issues, including sensitivity, false positive and false negative results, and ease of use of the BDS Oxygen Analyzer. You failed to follow your standard operating procedure, COS-QS-003, "Corrective and Preventive Action Systems," in that investigations were inadequate and no CAPAs were implemented. FDA requests that you provide information regarding the disposition of the remaining stock of the BDS product.

2. Failure to establish CAPA procedures for analyzing processes, work operations, concessions, quality records, service records, complaints, returned product, and other sources of quality data to identify existing and potential causes of nonconforming product and for identifying the action(s) needed to correct and prevent recurrences of nonconforming products or other quality problems [21 CFR 820.100(a)(1) and (2)]. Specifically, the standard operating procedure, COS-QS-003, "Corrective and Preventive Action Systems," was not followed in that:
 - a. Appropriate statistical methodology was not performed on customer complaints received during the period September 1, 2003 to August 19, 2004 regarding the BDS.
 - b. Analysis of customer complaints regarding defective devices manufactured between May 2003 and June 2004 did not capture quality trends that provided meaningful information.
3. Failure to establish procedures for receiving, reviewing, and evaluating complaints by a formally designated unit [21 CFR 820.198(a)]. Specifically, standard operating procedures, Procedure 600-005, "Product Occurrence Handling," and Procedure 600-165, "Parametric Analysis Guideline," were not followed. For example:
 - a. Investigation of customer complaint POR NA-2003-0803, regarding false negative results, did not include documentation of the findings.
 - b. Five (5) customer complaints (POR NA-2003-0767, POR NA-2003-0759, POR NA-2003-0803, POR NA-2003-0768, and POR NA-2003-0279) did not include documentation showing that the Device History Record (DHR) for the lot was reviewed or that the potential impact of the defect on other lots produced using the same manufacturing methods was evaluated.
4. Failure to validate processes, whose results cannot be fully verified by subsequent inspection and test, with a high degree of assurance, and failure to approve those processes according to established procedures [21 CFR 820.75(a)]. Specifically, the Sterilization Review Committee (SRC) concluded on 10/22/03 that the sterilization cycle employed for a non-approved product [REDACTED] would be acceptable for sterilization of the Enhanced Bacterial Detection System. There was no approved documentation to demonstrate that an evaluation was conducted to determine if the differences in ambient microbial loads, assessed differences in product density, or determined changes in components, such as changes in the number and formulation of the SPS tablets and in the tubing length, could impact the sterilization cycle and to determine if validation was required.

5. Failure to adequately establish and maintain procedures for verifying and validating device design [21 CFR 820.30(f) and (g)]. Specifically,
 - a. Documentation of the assay for the active ingredient in the SPS tablets was incomplete. Therefore, there was no confirmation that the design output met the design input requirements for the BDS.
 - b. There was no assurance that devices conformed to user needs and intended use. Specifically, there was no documentation that the test method used to assess tablet disintegration time of the SPS tablets used in the eBDS was performed under conditions of actual use.

In addition, our FDA investigators determined that you manufacture and distribute sterile, non-pyrogenic blood collection bags containing Anticoagulant Citrate Phosphate Double Dextrose Solution with AS-3 Nutricel Additive System. These products are drugs as defined by Section 201(g) of the Act [21 U.S.C. § 321(g)]. The FDA investigators documented a deviation from the Current Good Manufacturing Practices (CGMP) for Finished Pharmaceuticals, Title 21, Code of Federal Regulations, (CFR) Part 211. This deviation causes the drug product manufactured at your facility to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act (the Act). The violation from 21 CFR Part 211 was:

1. Failure to adequately maintain complete batch production and control records for each batch of drug products manufactured [21 CFR 211.188]. Specifically, during a Quality Control Inspection, units of lot [REDACTED] were found to have an incorrect lot number on the satellite bags. These units were subsequently reworked. However, the approved batch production record for lot [REDACTED] did not include any records generated prior to reworking of the product and did not include evidence of the [REDACTED] screening of the lot. You were cited for the same violation during the August 2002 inspection.

We acknowledge receipt of your written responses dated September 29, 2004, and November 9, 2004, describing the corrective measures your company has undertaken since the conclusion of the inspection and the discussion that took place upon issuance of the Form FDA 483. We have completed our review, and we have determined that your responses do not adequately address our concerns. For example:

1. Your response did not discuss whether or not you plan to initiate an investigation and a CAPA plan for the BDS. [FDA 483 Item #1]
2. We reviewed your Sterilization Review Committee document dated 10/22/03, which concluded that the sterilization process for the Bacterial Detection System (BDS) (product code 400-01) and [REDACTED] (product code 400-02) is adequate to assure the sterility of the Enhanced Bacterial Detection System (eBDS). However, you provided no documentation and data to support the following: [FDA 483 Item #3a]

- a. The committee's conclusion that the critical factors such as density and bioburden were substantially equivalent and would not influence the ability to deliver a lethal dose and achieve sterility with a high level of assurance.
 - b. The committee's conclusion that results of eBDS bioburden validation assays confirmed the differences between the BDS and eBDS products were insignificant.
3. Please explain how you determined that the results summarized in Attachment 1 of the document, "Assessment-Bacterial Detection System-Product Family "P" (430-41, demonstrate that these products have equivalent bioburdens. [FDA 483 Item #3b]
4. You stated that the tablet manufacturer performs the tablet disintegration test per the United States Pharmacopeia's (USP) test. As we state above, the test method did not represent the actual conditions. For this reason, your response is inadequate. [FDA 483 Item #4b]
5. Review of the 8/27/01 facsimile from the manufacturer of the SPS tablets for the BDS did not include a description of the test method or an approved written report. In addition, please provide a copy of procedure BBR-S0124-101100 (Rev. 1) referenced in Attachments 18-20 of your response. [FDA 483 Item #6]
6. You did not specify why an investigation of a customer's complaint did not include documentation of the findings. In addition, there was no documentation showing that the DHR for the lot was reviewed in the investigation of 5 other complaints. There was also no documentation that an analysis of the potential impact of the defects on other lots was performed during the investigation of these 5 complaints. [FDA 483 Item #10]
7. Please provide additional information demonstrating how your new standard operating procedure, COS-QS-001, "Management Review," will allow you to establish CAPA procedures and capture meaningful quality trends. [FDA 483 Item #11]
8. This is a repeat violation. While it is certainly important to revise standard operating procedures as necessary, our primary concern is that your established procedures are often not followed. [FDA 483 Item #16]

Please be reminded that all documentation relating to a specific product should be available for examination during inspections.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the Form FDA 483 issued at the conclusion of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance system. You are responsible for investigating and determining the causes of the

violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

Federal Agencies are advised of the issuance of all Warning Letters pertaining to medical devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submissions for devices to which the GMP deficiencies are reasonably related will be cleared until the violations have been corrected. Also, no requests for a Certificate For Exportability will be approved until the violations related to the subject devices have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

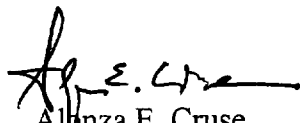
You should notify this office within fifteen (15) working days of receipt of this letter of the specific steps you have taken to correct the noted violations including an explanation of each step being taken to identify and prevent the recurrence of similar violations. If corrective action cannot be completed within (15) working days, state the reason for the delay and the time within which the corrections will be completed.

If you have any questions regarding this letter, please contact Ms. Mariza M. Jafary, Compliance Officer at 949-608-2977.

Your written reply should be addressed to:

Pamela Schweikert
Director, Compliance Branch
Food and Drug Administration
19701 Fairchild
Irvine, CA 92612-2446

Sincerely,



Alonza E. Cruse
District Director

Cc: State Department of Public Health
Environmental Health Services
Attn: Chief Food and Drug Branch
601 North 7th Street, MS-35
Sacramento, CA 94234-7320